REMARKS

Claims 15 and 17-19 are currently pending in this application. Claims 1-14, 16, and 20-46 were previously canceled without prejudice or disclaimer as to the subject matter of the canceled claims. Applicants respectfully reserve the right to pursue the canceled subject matter in one or more divisional or continuation applications. Upon entry and consideration of this response, claims 15 and 17-19 will remain pending.

Rejections

Rejections under 35 U.S.C. § 102(e)

Claims 15 and 16 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by the disclosure of Glazer *et al* (U.S. Patent No. 6,649,376). The Office Action states that Glazer *et al* teaches a fusion protein containing a phycobiliprotein, which may have one or more functional bilin domains, and that the first or second domain of the fusion protein may be a substrate for an enzyme, which will naturally modify the phycobiliprotein (column 3, lines 47-62).

Applicants respectfully disagree and traverse this rejection.

Applicants respectfully note that the subject matter of claim 16 was incorporated into the recitation of claim 15 in Applicants' amendment filed August 03, 2004. Therefore, Applicants' response will address this rejection as it pertains to amended claim 15, with the understanding that amended claim 15 incorporates and recites the subject matter of canceled claim 16.

In order for a reference to anticipate a claim, the reference must teach each element of that claim. Applicants submit that Glazer *et al* (U.S. Patent No. 6,649,376) does not teach each of the elements of amended claim 15. More specifically, claim 15 recites

> [i]n a method for biologic activity assays to determine a particular entity which induces a known biologic effect, the improvement comprising using a detectable label which is a fusion protein containing a phycobiliprotein domain and a second domain which undergoes the known biologic effect upon encountering the particular entity, wherein the known biologic effect induces a detectable change in the fusion protein and wherein the biologic activity assay is an assay for an enzyme and the second domain serves as a substrate for the enzyme.

Claim 15 clearly requires the presence of two separate domains in the fusion protein, wherein the first domain is represented by a phycobiliprotein domain. The second domain serves as a substrate for the enzyme.

As provided in the application as originally filed, "[p]hycobiliprotein domains may include all or part of the sequence of a phycobiliprotein subunit, or may correspond to the tertiary structure of a portion of a phycobiliprotein produced by a plurality of fragments of the phycobiliprotein sequence connected by spacer peptide sequences which permit folding to replicate the phycobiliprotein structure. Preferably, phycobiliprotein domains will be associated with prosthetic groups (e.g., chromophores) as necessary for fluorescence. Of course, most phycobiliprotein linker domains would not be expected to have bilin prosthetic groups associated with them." *See* specification, page 8, lines 1-8 (emphasis added).

Applicants submit that a "domain" is part of a protein (polypeptide), and by definition a prosthetic group cannot be a domain by itself. See, for example, Dorland's Illustrated Medical dictionary (available at www.mercksource.com) which defines a domain as "a compact globular structure composed of one section of a polypeptide chain that constitutes a recognizable unit of the tertiary structure of a protein." A paper copy of this definition is located in the attached Appendix. Applicants further submit that a phycobiliprotein "domain" is part of a protein (polypeptide), and a prosthetic group is not a domain by itself according to Applicants' teachings. As is clear from Applicants' disclosure, bilin prosthetic groups are associated with the phycobiliprotein domains of Applicants' disclosure but are not considered domains that are separate from the phycobiliprotein domains for purposes of Applicants' invention as claimed. Therefore, as bilins are not separate domains distinct from the phycobiliprotein domains, but instead are included as part of the phycobiliprotein domains, bilins cannot act as a second domain within the teachings of Applicants' disclosure.

The bilins as disclosed by Glazer *et al* do not function in Applicants' claimed invention as a "second" domain, and therefore the "second domain" of the present claims is not present in Glazer *et al.* Applicants submit that Glazer *et al* does not stand as an anticipatory reference under 35 U.S.C. § 102(e). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 15 under 35 U.S.C.§ 102(e).

Rejections under 35 U.S.C. § 103

Claims 17-19 were rejected under 35 U.S.C. § 103 as allegedly unpatentable over Bryan *et al* (U.S. Patent No. 6,232,107). The Office Action states that Bryan *et al* teaches fusion proteins and utilizing luciferase as a second domain that is able to catalyze substrates to produce

a detectable change (column 31, lines 65-66 and column 32, lines 1-10). The Office Action further states that it would have been obvious to one of ordinary skill in the art to modify the disclosure of Bryan *et al* to include using known enzymes such as a ribozyme, phosphokinase or a protease in these various methods and detection systems taught by the instant reference. According to the Office Action, it would have been *prima facie* obvious for one of ordinary skill in the art to substitute the known enzymes of claims 17-19 in the given assay parameters to assess biological activity as a means of optimizing the assays provided by the art.

Applicants respectfully disagree and traverse this rejection.

In considering whether a claimed invention is obvious, the four factual inquiries as enunciated in *Graham v. John Deere Co.* are used as a background in this consideration. The four factual inquiries are:

(A) Determining the scope and contents of the prior art;
(B) Ascertaining the differences between the prior art and the claims in issue;
(C) Resolving the level of ordinary skill in the pertinent art; and
(D) Evaluating evidence of secondary considerations.

Graham v. John Deere, 383 U.S. 1, 148 USPQ 459 (1966); MPEP § 2141. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *See* MPEP 2143.03.

Applicants note that the Office Action characterizes Bryan *et al* as teaching fusion proteins and utilizing luciferase as a second domain that is able to catalyze substrates to produce a detectable change. The Office Action further states that it would have been obvious to one of ordinary skill in the art to modify the reference of Bryan *et al* to include using known enzymes such as a ribozyme, phosphokinase or a protease.

However, Applicants respectfully submit that this characterization of Bryan *et al* misses the point, because independent claim 15, as amended on August 03, 2004, requires in part that the biological activity assay is an assay for an enzyme and *the second domain serves as a substrate for the enzyme*. The currently pending claims require that the fusion protein include a substrate for the enzyme, and not the enzyme itself. Dependent claims 17-19 do not change this requirement.

Applicants further respectfully note that the Examiner has previously stated that "the reference of Bryan *et al* does not teach that the second domain serves as a substrate for an

enzyme. The reference of Bryan *et al* teaches that the second domain in the fusion protein is luciferase, which is an enzyme." *See* Office Action dated May 04, 2004, section entitled "Response to Arguments", number 8. Therefore, one difference between the cited prior art and the present claims (the second Graham factor) is that the prior art teaches an enzyme as a "second domain", which is not encompassed by the claims. The Office Action does not present an analysis of this difference between the prior art and the claims in issue.

Applicants have provided at least one substantial difference between the claimed invention and the prior art, namely the inclusion of an enzyme substrate as the second domain of the fusion protein. The Office Action does not indicate where in the teachings of Bryan *et al* there is a suggestion to modify their own teachings to produce the claimed invention. The obviousness rejection is also silent to other references in the prior art teaching or suggesting all of the claim elements. As the claim elements are not taught or suggested by Bryan *et al*, Applicants submit that a *prima facie* showing of obviousness has not been presented.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 17-19 under 35 U.S.C. § 103 as allegedly unpatentable over Bryan *et al* (U.S. Patent No. 6,232,107).

CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

HUNTON & WILLIAMS LLP

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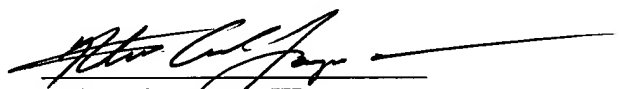
By: 

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